

To: Lowit, Anna[Lowit.Anna@epa.gov]; Reaves, Elissa[Reaves.Elissa@epa.gov]; Keigwin, Richard[Keigwin.Richard@epa.gov]; Akerman, Gregory[Akerman.Gregory@epa.gov]
From: Vogel, Dana
Sent: Wed 9/20/2017 2:56:06 PM
Subject: Fwd: Analysis that we just published "How well can carcinogenicity be predicted by high throughput "characteristics of carcinogens" mechanistic data?"
[Tox21 COCs Do Not Predict Cancer Becker et al 2017.pdf](#)
[ATT00001.htm](#)

FYI

Sent from my iPhone

Begin forwarded message:

From: "Becker, Rick" <Rick_Becker@americanchemistry.com>
To: "Vogel, Dana" <Vogel.Dana@epa.gov>
Subject: Analysis that we just published "How well can carcinogenicity be predicted by high throughput "characteristics of carcinogens" mechanistic data?"

Dear Dana,

I'd like to bring to your attention our recent paper "How well can carcinogenicity be predicted by high throughput "characteristics of carcinogens" mechanistic data?" It is an open access article and can be freely distributed to your EPA colleagues. A pdf version is attached. The paper can be accessed on line at <http://www.sciencedirect.com/science/article/pii/S0273230017302714?via%3Dihub>.

EPA IRIS seems to be adopting the IARC approach for using key characteristics of carcinogens (KCC) from high throughput screening (HTS) assays and other types of studies as mechanistic evidence for classification of chemicals. In essence, this approach is based on implied and unverified inference – that bioactivity detected in assays putatively measuring a KCC indicates high likelihood a substance is carcinogenic.

So we decided to explicitly test how well such HTS data predict cancer classifications. Substances that USEPA OPP previously classified as having cancer hazard potential were

designated as positives and substances OPP determined do not pose a carcinogenic hazard were designated as negatives. We downloaded HTS (ToxCast/Tox21) data for these substances and then sorted the results into 7 KCC (data for the other 3 KCC were not available); we used the exact same approach for assigning assays to KCCs as IARC. We then analyzed the dataset using an extensive array of statistics and machine learning algorithms. We found that the ability to predict cancer hazard for each KCC, alone or in combination, was no better than chance. Thus, concluding there's little scientific confidence in inference models derived from current ToxCast/Tox21 assays for KCC to predict cancer. Accordingly, in the paper, we recommend an improved approach for integrating such mechanistic data in cancer evaluations.

Please don't hesitate to contact me if you have any questions on the analysis or conclusions reached in our publication.

Sincerely

Richard A. Becker Ph.D. DABT | American Chemistry Council

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